

## REMARKS

Claims 1-46 are pending in the application. Claims 1-12, 22-40, 45, and 46 were withdrawn from consideration pursuant to a Restriction Requirement, leaving claims 13-21 and 41-44 subject to examination. The Information Disclosure Statement submitted on September 7, 2005 was not considered. The specification was objected to for using the abstract of the corresponding PCT application. Claims 13-21 and 41-44 were rejected under 35 U.S.C. § 101, 35 U.S.C. § 112, first (enablement) and second paragraphs; 35 U.S.C. § 102(b); and 35 U.S.C. § 102(e). Further, claims 43 and 44 were rejected under 35 U.S.C. § 112, first paragraph (written description). The objections and rejections are addressed below.

First, Applicant would like to provide a summary of certain central features of the invention, which may provide assistance to the Examiner in further consideration of this case. The present claims are drawn to libraries including a plurality of mixtures of peptides. In each mixture, the different positions with a peptide in the mixture (i.e.,  $X_1$ - $X_2$ - $X_3$ -...- $X_n$ ) are defined by being selected from particular groups of amino acids. The mixtures of the libraries are further defined by no peptide being present in more than one of the mixtures, and/or by the combination of groups chosen to obtain the peptides differing between the mixtures. Therefore, it is clear that the mixtures within the libraries contain distinct populations of peptides. This organization of the peptides within the library provides a level of organization that is not present in a library of peptides lacking such a structure. Further, as discussed below, this type of organization is not described in the references cited in this case.

#### Information Disclosure Statement

The Office Action states that the Information Disclosure Statement (IDS) filed on September 7, 2005 fails to comply with the requirements of 37 C.F.R. § 1.98(a)(1) because a Form PTO 1449 is not evident on file. Applicant submits herewith a copy of the IDS filed on September 7, 2005, which includes a Form PTO 1449. Also enclosed is a Patent Office stamped return receipt postcard listing the IDS and Form PTO 1449. Applicant requests that the IDS be considered and that an initialed copy of the Form PTO 1449 be returned with the next Action in this case.

#### Objection to the Specification

The specification was objected to for using the PCT abstract. This objection has been met by the present amendment to the specification, by which a separate abstract has been added as the last page of the specification.

#### Rejection under 35 U.S.C. § 101

Claims 13-21 and 41-44 were rejected under 35 U.S.C. § 101 on the basis that the claimed mixtures of peptides read on naturally occurring peptides. Applicant respectfully requests reconsideration and withdrawal of this rejection.

Before addressing the rejection, Applicant first notes that claim 13 has been amended to include the limitations of claims 15 and 18, which have been canceled. Claim 13 thus now specifies libraries of mixtures of peptides. As provided in amended claim 13, each position (i.e.,  $X_1-X_2-X_3-\dots-X_n$ ) within a peptide of a mixture is limited to a particular group of amino acids. In

particular, at each position of each peptide the amino acid is selected from one of four groups of five amino acids each, or one of two groups of ten amino acids each, in either case with no amino acid being present in more than one group. In view of these limitations, it is clear that the claimed libraries do not include peptides having all sequences possible based on a random selection from all 20 naturally occurring amino acids. Rather, the libraries of the present invention represent particular subsets of a random library of peptides.

In the rejection, the Office Action states that the claimed mixtures of peptides read on naturally occurring peptides, and that the claimed libraries lack patentable utility. In response, Applicant submits that the claimed libraries of mixtures do not read on naturally occurring peptides. As noted above, the peptides within the mixtures of the libraries are limited with respect to the sequences that they include. In particular, each position (i.e.,  $X_1$ - $X_2$ - $X_3$ -...- $X_n$ ) within a peptide of a mixture is limited to a group of amino acids (one of four groups of five amino acids each, or one of two groups of ten amino acids each, in either case with no amino acid being present in more than one group). Thus, the peptides of the mixtures of the libraries represent a subset of all possible peptides, and are designed by the specified parameters. Applicant is not aware of the existence of such libraries in nature, and no reference has been cited showing the existence of such libraries. The claims thus do not read on naturally occurring peptides.

The Office Action further states that the claimed libraries lack patentable utility, that there is no novelty in compiling or collecting known compounds, and that if the mixtures are useful as screening tools, then methods of using the mixtures may be more appropriate to claim. In response, Applicant submits that, as discussed above, the presently claimed libraries do not

exist in nature. Rather, the libraries include novel mixtures of peptides designed based on particular parameters, and the design of the libraries provides benefits with respect to the level of complexity of the libraries when used in screening methods (see page 23 of the specification). Further, Applicant notes that the specification provides detailed information as to how to make and use the claimed libraries of mixtures in screening methods (see, e.g., pages 22-28). This description supports the utility of the claimed libraries themselves, as well as claims to methods of their use in screening.

In view of the above, Applicant requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claims 13-21 and 41-44 were rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. The Office Action states that although the specification enables antigenic amino acids selected from Group 1 (charged), Group 2 (small hydrophobic), Group 3 (large hydrophobic), and Group 4 (hydrophilic), it does not enable groups of amino acids consisting of less than 20 different amino acids. Further in the rejection, the Office Action states that “the claimed number of groups would encompass a huge combination of different amino acids in a group hence, a potentially huge numbers of mixtures of peptides” and that “it is not clearly apparent from the huge scope of the claims the ones that would result in a peptide having a function.”

Applicant requests reconsideration and withdrawal of this rejection. The specification clearly describes how to make the claimed libraries, including by use of standard solid-phase

peptide synthesis (see, e.g., page 22-28 and Example 4). Whether certain peptides within the libraries are not “functional” is not an issue, as any such peptides would simply not be recognized by an antibody within a test sample, and thus would be of no consequence. However, having a large number of peptides with different sequences in a library will ensure that an optimal number of possible sequences within a given set of parameters are represented, to maximize antibody recognition and antigen identification. The application thus describes how to make and use the claimed libraries. Applicant therefore submits that the claims are enabled and requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph (written description)

Claims 43 and 44 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Applicant requests reconsideration and withdrawal of these rejections for the reasons set forth below.

In reference to claim 43, the Office Action states that a kit comprising antibodies specific for two or more immunoglobulin subclasses is not supported in the original disclosure. In response, Applicant points to page 38, line 3, where it is stated in reference to kits of the invention that “...any labeled antibodies described herein may be used.” Antibodies specific for two or more immunoglobulin subclasses are described, for example, at page 27, lines 1-2, where it is stated that “...an antibody capable of detecting two, more or all of these antibody sub-classes and subtypes can be used.” In view of this support, Applicant requests that this rejection be withdrawn.

In reference to claim 44, the Office Action states that a kit comprising a peptide of the

specified formula and a labeled antibody is not supported in the specification as filed. In response, Applicant points to page 38, lines 2-3, where it is stated that “[a]ny antigens, mixture of antigens or library of antigens as described herein may be used in such a kit. Similarly, any labeled antibodies described herein may be used.” The formula specified in claim 44 is set forth in the specification at pages 24-25. In view of this support, Applicant requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 13-21 and 41-44 were rejected under 35 U.S.C. § 112, second paragraph for indefiniteness on several grounds, which are addressed as follows.

Claim 13 was rejected for being drawn to a mixture of peptides, which the Office Action states is the same as the library of claim 18, making these claims substantial duplicates. This rejection is moot because, as discussed above, the limitations of claim 18 (as well as claim 15) have been incorporated into claim 13, and claims 18 and 15 have been canceled. For the record, Applicant notes that the scope of claims 13 and 18 prior to the present amendment differ, as claim 13 specified peptide mixtures limited by certain parameters, while claim 18 specified a library of such mixtures, with the mixtures within the library potentially differing from one another with respect to parameters required to be the same within a mixture. Applicant requests that this rejection be withdrawn.

Claim 13 was also rejected, with the Office Action stating that the recitation that “each group of amino acids consists of less than 20 different amino acids” is inconsistent with the recitation that “all of the following amino acids are present in at least one group: arginine, lysine

etc.” In response, Applicant notes that claim 13 now specifies that each group contains either five or ten amino acids, and such groups can thus certainly not include all 20 amino acids. However, all 20 amino acids can be represented in the mixtures, as more than one group is used in making the peptides of the mixtures. Thus, for example, in the case of a mixture made up of peptides having amino acids from two groups of ten, one group of ten amino acids can include 10 of the naturally occurring amino acids and the other group of ten amino acids can include the other 10 of the naturally occurring amino acids, resulting in all 20 naturally occurring amino acids being represented in the mixtures (but not in each group). In other words, all 20 naturally occurring amino acids can be represented in the groups because even though each group cannot include all 20, there are multiple groups including subsets of the amino acids. This point has been emphasized by the present amendment to claim 13, by which the claim now specifies that “all of the following amino acids are present in a combination of the four groups of five amino acids or the two groups of ten amino acids: arginine, lysine...”

The Office Action further states that if all peptides are of the same length and at least one group contains all of the 20 amino acids, it is not clear as to the sequence of the other groups. As stated above, claim 13 specifies that the groups are of either 5 or 10 amino acids, and thus an individual group cannot include all 20 amino acids. Applicant thus requests that this rejection be withdrawn.

Claim 13 was further indicated as being confusing for reciting “...for each peptide in the mixture the amino acid at the same position is selected from the same group,” on the basis that it is unclear which position is being referred to. In response, Applicant notes that claim 13 has been amended to specify that each position refers to one of  $X_1$ - $X_2$ - $X_3$ -... $X_n$ . Thus, the “same

position” when used in reference to multiple peptides means position  $X_1$  of each of the peptides, position  $X_2$  of each of the peptides, etc. Applicant thus requests that this rejection be withdrawn.

Claim 41 was rejected as being unclear as to the binding of antibodies to immunoglobulins. In particular, the Office Action questions whether the binding is to an antigen recited in (i) or to immunoglobulins of no antecedent basis. In response, Applicant submits that the kit of claim 41 can be used in a method for identifying antibodies present in a sample. In one example of such a method, a library of peptide antigens is contacted with a serum sample and antibodies in the sample recognizing antigens of the library are bound to library components. The bound antibodies can then be visualized by use of labeled antibodies recognizing immunoglobulins. This general method is described throughout the specification (see, e.g., page 7, line 27 through page 8, line 2; and in particular page 29 through page 30, line 2). Returning to the issue raised in the rejection, Applicant submits that the term “immunoglobulin” does not have antecedent basis in claim 41, and the binding, which is not indicated as being directed against the antigen recited in (i), is not intended to be so directed. Rather, the binding is to immunoglobulins, as would be carried out in the method described above. Applicant thus requests that this rejection be withdrawn.

Further in this rejection, the Office Action questions “the differentiating characteristics of a plurality or a mixture of antigens.” In response, Applicant submits that the meaning of “a plurality of antigens” is clear, in that it indicates multiple antigens. As to the term “mixture,” this is a term that is specifically defined in the application, as discussed in detail above, and it refers to peptides including sequences created by selection from particular groups, etc. Applicant thus requests that this rejection be withdrawn.



Claim 42 was rejected on the basis that it is not clear when the plurality of antigens comprises alternatively an oligopeptide alone or together in combination with oligosaccharides. In response, Applicant submits that the claim covers kits in which the antigens comprise oligopeptides alone, oligosaccharides alone, and mixtures of oligopeptides and oligosaccharides. The claim has been amended to make this clearer.

Claim 44 was rejected for depending from a non-elected method claim. As claim 44 does not depend from a method claim, Applicant has considered this rejection in reference to claim 41, which, prior to the present amendment, depended from a non-elected method claim. Claim 41 has now been amended to depend from claim 13, which is an elected claim.

Claims 41-44 were rejected as being indefinite as to the components of the kit such that the kit can be used for its intended purpose, with the Office Action making reference to instructions as to the use of the kit. In response, Applicant submits that the claims are not indefinite, as they clearly set forth components that are comprised within the claimed kits. Applicant thus requests that this rejection be withdrawn.

#### Rejections under 35 U.S.C. § 102

Claims 13-21 were rejected under 35 U.S.C. § 102(b) as being anticipated by Houghten et al., Nature 354:84-86, 1991 or Devlin et al., Science 249:404-406, 1990; claims 13-21 and 41-44 were rejected under 35 U.S.C. § 102(e) as being anticipated by Fowlkes et al., U.S. Patent No. 6,617,114; claims 13-21 and 41-44 were rejected under 35 U.S.C. § 102(b) as being anticipated by Lynch et al., U.S. Patent No. 5,962,244; and claims 13-21 were rejected under 35 U.S.C. § 102(b) as being anticipated by Lam et al., U.S. Patent No. 5,858,670. Applicant requests

reconsideration and withdrawal of these rejections for the following reasons.

The Office Action states that the presently claimed mixtures and libraries have no defined structures and sequences. In response, and as discussed in detail above, Applicant submits that the claimed libraries are not completely random. Rather, the libraries are limited with respect to complexity, based on the requirement that the amino acids of the peptides of the mixtures be selected from particular groups of amino acids.

The cited references describe libraries of peptides of including random amino acid sequences. In certain instances, particular positions of the peptides may be specified as having particular sequences, with the remaining being random, while in other instances, the lengths of the peptides are specified as being within particular ranges (see, e.g., the cited passages of Fowlkes). None of the references describes a library including mixtures of peptides characterized in that each position of the peptides is limited to a subset of the 20 naturally occurring amino acids (e.g., a subset of five or ten, as discussed above). Thus, as the references do not describe this central feature of the presently claimed invention, Applicant submits that these rejections should be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges not covered or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: October 27, 2008

Susan M. Michaud

Susan M. Michaud, Ph.D.

Reg. No. 42,885

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045